UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,005	03/26/2004	Dana P. Gaddy	022438.45889	7761

28172 7590 09/06/2006

BUTLER, SNOW, O'MARA, STEVENS & CANNADA PLLC
6075 POPLAR AVENUE
SUITE 500
MEMPHIS, TN 38119

EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,005	GADDY, DANA P.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20040517*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The Information Disclosure Statement (IDS) filed 17 May 2004 is acknowledged. Applicant's amendment of the claims filed 27 July 2006 has been entered.

Election/Restrictions

Applicant's election of Group III, claims 19-22, without traverse, in the response received on 27 July 2006 is acknowledged.

Claims 1-22 are pending. Claims 1-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 19-22 are under examination.

Information Disclosure Statement

The references listed "Other Documents" section in the Form PTO-1449 on the information disclosure statement filed 17 May 2004 are lined through since they are improper. Specifically, they don't provide Journal, volume and page numbers. They were considered, however, the printer has been directed not to print these citations on the face of the patent.

Claim Objections

Claims 19 and 21 are objected to because of the following informalities: the claims recite a method step "comprising: a.". There is only one method step, and therefore, "a." is not necessary. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-22 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to a method to increase cancellous bone strength or to increase bone volume in a mammal comprising administering a derivative of inhibin to the mammal, wherein said derivative of inhibin is selected from the group consisting of a polypeptide and a small molecule agonist. What applicant has described in the specification is a correlation that a decrease in circulating inhibin levels contributes to bone loss in pre-, peri-, and post-menopausal women, and that inhibin-A and inhibin-B act to suppress bone turnover and maintain bone mass through direct inhibitory effects on osteoblast and osteoclast development. Applicant has not described the genus of inhibin derivatives that has the same property. Applicant describes in [0052] that the derivative of inhibin can be protein, peptide or polypeptide, or a small molecule agonist. However, there is no teaching regarding the relationship of structure to function, such as what structure feature these molecules have. Thus, the claims encompass a genus of

molecules, which vary substantially in composition, and could have very different structural and functional characteristics from the conjugation products that Applicant has disclosed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making of the claimed product, or any combination thereof. In this case, there is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of peptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement

that is part of the invention and reference to a method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only inhibin-A and inhibin-B, but not the full scope of the claimed derivatives of inhibin, is adequately described in the disclosure.

Claims 19-22 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method to increase cancellous bone strength or to increase bone volume in pre-, peri-, and post-menopausal women, comprising administering inhibin-A or inhibin-B to the women, does not reasonably provide enablement for a method comprising administering any derivative of inhibin to any mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims are directed to a method to increase cancellous bone strength or to increase bone volume in a mammal comprising administering a derivative of inhibin to the mammal, wherein said derivative of inhibin is selected from the group consisting of a polypeptide and a small molecule agonist. The claims are broad in that they encompass administering any derivative of inhibitin to any mammal subject. The specification

discloses a method to suppress bone turnover and maintain bone mass in pre-, peri-, and post-menopausal women by administering to the patients inhibin-A or inhibin-B, which acts through direct inhibitory effects on osteoblast and osteoclast development. The specification, however, does not provide any guidance for making or using other derivatives of inhibin, nor in any mammal subject. The "bigenic" mouse model used in the in vivo study (Example 4) does not support the use of the method for any mammal since it is a genetically manipulated system. Also, the specification defines "a derivative of inhibin" as a molecule of a protein, a peptide or a polypeptide, or a small molecule agonist, that is capable of binding inhibin receptors and/or initiating the targeted inhibin [0052]. Thus, the claims encompass a genus of molecules, known or unknown, with a diverse range of structures and functions. The specification does not provide any teaching regarding the relationship of structure to function, such as what structure feature these molecules have. Further, not all molecules that have the binding activity to inhibin receptors can be used in the therapeutic uses as recited in the claims. For example, Wiater et al. (J. Biol. Chem., 2006, 281(25):17011-17022) teach that Betaglycan is a co-receptor that mediates signals by TGF β superfmily members, including the distinct and often opposed actions of TGFβs and inhibins (see abstract). Wiater et al. states that the functional consequences of inhibin boinding to betaglycan are diametrically opposed to the events that occur subsequent to TGFβ binding (pp. 17011, right column, 2nd paragraph). While the prior art (U.S. Patent No: 5,674,844) describes the same molecules, it fails to provide compensatory guidance. Since the claims encompass a large genus of molecules with no requirement for structure and

function, and the specification does not define what these molecules will be, one of skill in the art would evaluate all non-exemplified polymer-conjugated proteins for therapeutic uses. Thus, undue experimentation would be required for the artisan to make and use the invention as broadly claimed.

Due to the large quantity of experimentation necessary to generate the nearly infinite number of derivatives of inhibin recited in the claims and screen same for therapeutic uses in any mammal, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide therapeutic uses in any mammal, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of protein structure on function, and the breadth of the claims which fails to recite any structural and functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Kuberasampath et al. (U.S. Patent No: 5,674,844, issued in 1997). The '844 patent

teaches a method for increasing bone mass, or preventing bone loss in an individual afflicted with a bone disease which includes administering to the individual a therapeutically effective amount of morphogen (column 3, lines 16-25). The '844 patent teaches treating diseases that result in loss of bone mass, such as osteoporosis (column 3, line 62 through column 4, line 5). The '844 patent teaches that particular useful sequences for use as morphogens include the inhibins/activin proteins (column 12, lines 52-54). The '844 patent teaches formulations that comprising a pharmaceutically acceptable carrier (column 23, lines 108). Therefore, the '844 patent anticipates the instant claims.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph. D.
August 31, 2006

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600